# Complete Summary

## GUIDELINE TITLE

Venous thromboembolism prophylaxis.

## BIBLIOGRAPHIC SOURCE(S)

Institute for Clinical Systems Improvement (ICSI). Venous thromboembolism prophylaxis. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2005 Jun. 45 p. [80 references]

## GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Venous thromboembolism prophylaxis for surgical/trauma patients. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2003 Oct. 39 p.

## COMPLETE SUMMARY CONTENT



## SCOPE

### DISEASE/CONDITION(S)

Venous thromboembolism

### GUIDELINE CATEGORY

Prevention
Risk Assessment

### CLINICAL SPECIALTY

Anesthesiology
Emergency Medicine
Family Practice
Hematology
Internal Medicine
Orthopedic Surgery
Preventive Medicine
Pulmonary Medicine
Surgery

## INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Health Care Providers
Health Plans
Hospitals
Managed Care Organizations
Nurses
Physician Assistants
Physicians

## GUIDELINE OBJECTIVE(S)

- To increase the percentage of hospitalized adult patients (18 years and older) who are appropriately screened for venous thromboembolism (VTE) risk
- To increase the percentage of hospitalized adult patients (18 years and older) who are at risk of VTE who have received education for VTE that includes: VTE risk signs and symptoms and treatment/prophylaxis methods available
- To increase the percentage of hospitalized adult patients who begin early and frequent ambulation to reduce VTE risk
- To increase the percentage of hospitalized adult patients (18 years and older) receiving appropriate pharmacological and/or mechanical prophylaxis treatment

## TARGET POPULATION

Adult (18 years and older) hospitalized patients

## INTERVENTIONS AND PRACTICES CONSIDERED

1. Assessment of venous thromboembolism (VTE) risk including procedure-related risk and patient-related risk
2. VTE prophylaxis for low-risk patients including patient education and early ambulation
3. VTE prophylaxis for moderate- and high-risk patients including patient education, early ambulation, elastic stockings, intermittent pneumatic compression (IPC) if immobilized, and anticoagulant prophylaxis (low-dose unfractionated heparin [LDUH] and low molecular weight heparin [LMWH - enoxaparin and dalteparin]) unless contraindicated.

   Note: Aspirin is not recommended.

4. VTE prophylaxis for very high-risk patients including patient education, early ambulation, elastic stockings, intermittent pneumatic compression if immobilized, and anticoagulant prophylaxis (low molecular weight heparin, fondaparinux, and adjusted dose of warfarin)

   Note: Aspirin and low-dose unfractionated heparin are not recommended.

5. Assessment of the need for post-discharge anticoagulation

MAJOR OUTCOMES CONSIDERED

- Incidence and prevalence of venous thromboembolism in hospitalized patients undergoing procedures or suffering significant trauma
- Rate of thromboembolic events including pulmonary embolism in patients on low molecular weight heparin (LMWH) versus low dose unfractionated heparin (LDUH)
- Rate of perioperative death in patients on LMWH versus LDUH
- Rate of intraoperative and postoperative bleeding (major and minor) in patients on LMWH versus LDUH

## METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Key conclusions (as determined by the work group) are supported by a conclusion grading worksheet that summarizes the important studies pertaining to the conclusion. Individual studies are classed according to the system presented below, and are designated as positive, negative, or neutral to reflect the study quality.

Conclusion Grades:

Grade I: The evidence consists of results from studies of strong design for answering the question addressed. The results are both clinically important and consistent with minor exceptions at most. The results are free of any significant doubts about generalizability, bias, and flaws in research design. Studies with negative results have sufficiently large samples to have adequate statistical power.

Grade II: The evidence consists of results from studies of strong design for answering the question addressed, but there is some uncertainty attached to the conclusion because of inconsistencies among the results from the studies or because of minor doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from weaker designs for the question addressed, but the results have been confirmed in separate studies and are consistent with minor exceptions at most.

Grade III: The evidence consists of results from studies of strong design for answering the question addressed, but there is substantial uncertainty attached to the conclusion because of inconsistencies among the results of different studies or because of serious doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from a limited number of studies of weak design for answering the question addressed.

Grade Not Assignable: There is no evidence available that directly supports or refutes the conclusion.

Study Quality Designations:

The quality of the primary research reports and systematic reviews are designated in the following ways on the conclusion grading worksheets:

Positive: indicates that the report or review has clearly addressed issues of inclusion/exclusion, bias, generalizability, and data collection and analysis.

Negative: indicates that these issues (inclusion/exclusion, bias, generalizability, and data collection and analysis) have not been adequately addressed.

Neutral: indicates that the report or review is neither exceptionally strong nor exceptionally weak.

Not Applicable: indicates that the report is not a primary reference or a systematic review and therefore the quality has not been assessed.

Classes of Research Reports:

A. Primary Reports of New Data Collection:

Class A:

- Randomized, controlled trial

Class B:

- Cohort study

Class C:

- Non-randomized trial with concurrent or historical controls
- Case-control study
- Study of sensitivity and specificity of a diagnostic test
- Population-based descriptive study

Class D:

- Cross-sectional study
- Case series
- Case report

B. Reports that Synthesize or Reflect upon Collections of Primary Reports:

Class M:

- Meta-analysis
- Systematic review
- Decision analysis
- Cost-effectiveness analysis

Class R:

- Consensus statement
- Consensus report
- Narrative review

Class X:

- Medical opinion

## METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

## DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

## METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

## RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

## COST ANALYSIS

The guideline developers reviewed published cost analyses.

## METHOD OF GUIDELINE VALIDATION

Clinical Validation-Pilot Testing
Internal Peer Review

## DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

### Institute Partners: System-Wide Review

The guideline annotation, discussion, and measurement specification documents undergo thorough review. Written comments are solicited from clinical, measurement, and management experts from within the member groups during an eight-week review period.

Each of the Institute's participating member groups determines its own process for distributing the guideline and obtaining feedback. Clinicians are asked to suggest modifications based on their understanding of the clinical literature coupled with their clinical expertise. Representatives from all departments involved in implementation and measurement review the guideline to determine its operational impact. Measurement specifications for selected measures are developed by the Institute for Clinical Systems Improvement (ICSI) in collaboration with participating member groups following implementation of the guideline. The specifications suggest approaches to operationalizing the measure.

### Guideline Work Group

Following the completion of the review period, the guideline work group meets 1 to 2 times to review the input received. The original guideline is revised as necessary, and a written response is prepared to address each of the responses received from member groups. Two members of the Cardiovascular Steering Committee carefully review the input, the work group responses, and the revised draft of the guideline. They report to the entire committee their assessment of four questions: (1) Is there consensus among all ICSI member groups and hospitals on the content of the guideline document? (2) Has the drafting work group answered all criticisms reasonably from the member groups? (3) Within the knowledge of the appointed reviewer, is the evidence cited in the document current and not out-of-date? (4) Is the document sufficiently similar to the prior edition that a more thorough review (critical review) is not needed by the member group? The committee then either approves the guideline for release as submitted or negotiates changes with the work group representative present at the meeting.

### Pilot Test

Member groups may introduce the guideline at pilot sites, providing training to the clinical staff and incorporating it into the organization's scheduling, computer, and

other practice systems. Evaluation and assessment occur throughout the pilot test phase, which usually lasts for three-six months. At the end of the pilot test phase, ICSI staff and the leader of the work group conduct an interview with the member groups participating in the pilot test phase to review their experience and gather comments, suggestions, and implementation tools.

The guideline work group meets to review the pilot sites' experiences and makes the necessary revisions to the guideline, and the Cardiovascular Steering Committee reviews the revised guideline and approves it for release.

## RECOMMENDATIONS

### MAJOR RECOMMENDATIONS

The recommendations for venous thromboembolism (VTE) prophylaxis are presented in the form of 2 algorithms with 18 components, accompanied by detailed annotations. Algorithms are provided for Venous Thromboembolism Prophylaxis for Hospitalized Surgical/Trauma Patients and Venous Thromboembolism Prophylaxis for Hospitalized Medical Patients; clinical highlights and selected annotations (numbered to correspond with the algorithm) follow.

Class of evidence (A-D, M, R, X) and conclusion grade (I-III, Not Assignable) definitions are provided at the end of the "Major Recommendations" field.

#### Clinical Highlights

1. All patients should receive proper education regarding venous thromboembolism (VTE) risk, signs and symptoms of VTE, and prophylaxis methods available. (Annotations #7, 9, 11, 15, 17, 18)
2. Early and frequent ambulation should be encouraged when possible in all patient groups. (Annotations #7, 9, 11, 15, 17, 18 )
3. Risk of VTE development continues beyond hospitalization, and the need for post-discharge anticoagulation should be assessed. (Annotations #9, 11, 17, 18)
4. All surgical/trauma patients who have moderate/high or very high-risk for VTE should receive anticoagulation prophylaxis unless contraindicated. (Annotations # 9, 11)
5. All medical patients who have a high risk for VTE should receive anticoagulation prophylaxis unless contraindicated. (Annotation #18)
6. Aspirin is not recommended for VTE prophylaxis because other methods are more effective. (Annotations #7, 11, 18)
7. For all patients receiving spinal or epidural anesthesia, precautions should be taken when using anticoagulant prophylaxis to reduce the risk of epidural hematoma. (Annotations #9, 11)

#### Venous Thromboembolism Prophylaxis for Hospitalized Surgical/Trauma Patients Algorithm Annotations

1. Adult Admitted to an Acute Care Hospital

The American College of Chest Physicians (ACCP) consensus recommends that all institutions develop a formal strategy that addresses the prevention of thromboembolic complications. This guideline is intended for patients who are undergoing procedures or have trauma that is associated with increased risk for venous thromboembolism (VTE). Appropriate prophylactic measures should be utilized whenever possible to minimize these risks and lower overall morbidity and mortality associated with this disease. Frequently encountered high-risk circumstances are best addressed with written protocols and order sets to standardize the care given to these types of patients.

4. Surgical Procedure/Trauma

Key Points:

- Patients undergoing surgical procedures or suffering significant trauma are at risk of developing venous thromboembolism.
- Appropriate prophylaxis measures should be initiated for patients based on risk for developing VTE.

All patients admitted for trauma or to undergo procedures should be evaluated for risk of VTE development. Appropriate prophylaxis measures should be initiated for patients deemed to be at risk.

Evidence supporting this recommendation is of class: R

5. Assess VTE Risk

Patients undergoing surgical procedures have VTE risks associated with the procedure such as:

- Site
- Surgical technique
- Duration
- Type of anesthesia
- Complications (infection, shock, etc.)
- Degree of immobilization

Procedures that are considered high-risk include:

- Major open abdominal or urologic surgery
- Cranial and spinal neurosurgical procedures
- Open gynecologic procedures

Lower extremity joint replacement and hip fracture repair are considered very high VTE risk in themselves.

Patients with trauma have VTE risks dependent on location and severity. Patients with multi-system, spinal cord, or lower extremity blunt trauma appear to be at very high-risk.

Refer to the original guideline document for other VTE risk factors that play an additive role and for guide to risk stratification.

Evidence supporting this recommendation is of class: R

7. Prophylaxis Plan for Low VTE Risk

Patients with a low risk of developing a VTE should receive patient education and early ambulation. Patient education should encourage early and frequent ambulation and flexion/extension exercises for the ankles. No specific measures are required beyond this.

All patients irrespective of their risk for VTE should receive patient education about VTE. Patient education should include VTE risk, signs and symptoms of VTE, and treatment/prophylactic measures available.

Evidence supporting this recommendation is of class: R

8. Moderate/High VTE Risk

Moderate VTE Risk

Moderate-risk patients include:

- Major surgery in those less than age 40 of age
- Minor surgery in those age 40 to 60
- Minor surgery in those less than age 40 with additional risk factors (prior VTE, cancer, hypercoagulability)

High VTE Risk

High risk patients include:

- Minor surgery in those over 60 years of age without additional risk factors
- Major surgery in those over 40 years of age without additional risk factors
- Minor surgery in those over 40 years of age with additional risk factors (prior VTE, cancer, hypercoagulability)

See "Other VTE risk factors that play an additive role" and "Guide to Risk Stratification" sections in Annotation #5 in the original guideline for patient related risk factors.

Without prophylaxis, moderate-risk VTE patients have a 2 to 4% proximal deep vein thrombosis (DVT) risk, 1 to 2% clinical pulmonary embolism (PE) risk, and a 0.1 to 0.4% risk of fatal PE.

Without prophylaxis, high-risk VTE patients have a 4 to 8% proximal DVT risk, 2 to 4% clinical PE risk, and a 0.4 to 1.0% risk of fatal PE.

Evidence supporting this recommendation is of classes: B, D, R

9. Prophylaxis Plan for Moderate/High VTE Risk

Key Points:

- Anticoagulation regimens are started 1 to 2 hours prior to surgery.
- Aspirin is not recommended as an anticoagulation regimen.
- Patients with increased risk of bleeding or contraindications to anticoagulation regimens should be considered for elastic stockings and intermittent pneumatic compression.

Contraindications to Antithrombotic Prophylaxis

a. Extreme thrombocytopenia
b. History of heparin-induced thrombocytopenia (HIT) is a contraindication for use of heparins.
c. Uncontrolled hypertension (systolic >200, diastolic >120)
d. Bacterial endocarditis
e. Active hepatitis or hepatic insufficiency
f. Other conditions that could increase the risk of bleeding

Moderate VTE Risk

All moderate VTE risk patients should receive patient education, early ambulation, elastic support stockings, intermittent pneumatic compression if immobilized, and anticoagulant prophylaxis unless contraindicated.

For short term prophylactic anticoagulation there are relatively few conditions with excessive bleeding risk or other considerations that would contraindicate anticoagulation. Acceptable anticoagulation regimens include low dose unfractionated heparin (LDUH) and low molecular weight heparin (LMWH). Aspirin is not recommended.

Acceptable anticoagulant regimens are started 1 to 2 hours prior to surgery and include LDUH subcutaneously every 8 hours or LMWH (enoxaparin and dalteparin.) For general surgery, non-orthopedic patients, aspirin is not recommended.

LDUH is cost effective and effective in reducing the risk of postoperative VTE in moderate-risk patients. While LMWH has the convenience of single day dosing, it is not superior to LDUH and is significantly more expensive. Further, overall complication rates appear similar between LDUH and LMWH.

Studies, primarily in patients over 40 years of age, have shown that LDUH is as effective as LMWH as an anticoagulant prophylaxis agent for moderate and high-risk surgical patients. [Conclusion Grade I: See Conclusion Grading Worksheet - Appendix A - Annotation #9 (Selecting Heparin) in the original guideline]

Anticoagulant regimens reduce compliance issues and have been shown to reduce the incidence of post-operative VTE. Three issues that need to be addressed are choice of agent, dosing, and duration of therapy.

For moderate-risk patients who do not have a contraindication to anticoagulation, the current choice is between LMWH and LDUH. Aspirin has not been shown to be an effective agent in general surgical patients.

In moderate-risk patients with contraindications to pharmacologic prophylaxis, elastic stockings and intermittent pneumatic compression may be considered an alternative to LDUH and LMWH, bearing in mind that there is less data to support this strategy, that hemorrhagic complications are low with both strategies, and that compliance may be a significant problem when relying on intermittent pneumatic compression alone for VTE prophylaxis. For short-term prophylactic anticoagulation, there are relatively few conditions associated with an excessive risk of bleeding or other significant considerations. When an epidural is used for anesthesia, it is most appropriate to wait until the catheter is removed before starting pharmacologic prophylaxis. See Annotation #9 under Neuraxial Blockade for general guidelines on epidural anesthesia.

Evidence supporting this recommendation is of classes: A, C, M, R

High VTE Risk

All high VTE risk patients should receive patient education, early ambulation, elastic support stockings, intermittent pneumatic compression if immobilized, and anticoagulant prophylaxis unless contraindicated. For short term prophylactic anticoagulation there are relatively few conditions with excessive bleeding risk or other considerations that would contraindicate anticoagulation. Acceptable anticoagulation regimens include LDUH and LMWH. Aspirin is not recommended.

Without prophylaxis, high-risk category patients have VTE rates ranging from 20% to 40%. The risk of PE ranges from 2% to 4%, with 0.4% to 1.0% of patients having a fatal PE.

Although no specific studies exist to document the value of patient education and early ambulation to reduce VTE risk, the work group believes these measures are important for VTE risk patients, including those in the high-risk group.

Refer to the Table in Annotation #9 of the original guideline document for details on pharmacotherapy for patients stratified to high-risk of VTE.

Supportive Statements for Pharmacotherapy of High VTE Risk Patients:

1. For most general surgery patients, LDUH remains the agent of choice. LMWH has been found to be as safe and effective yet remains significantly more expensive.

2. In general surgery, patients may receive preoperative heparin without increased risk of bleeding.
3. LMWHs cause less heparin-induced thrombocytopenia (HIT) than LDUH. There is early evidence to support the use of fondaparinux in HIT although further confirmatory studies are needed.
4. LMWH should be adjusted at prophylactic doses for patients with a creatinine clearance less than 30 mL/minute. The manufacturer recommended dose of enoxaparin is 30 milligrams daily in this population; the manufacturer of dalteparin does not list a similar dose recommendation.
5. In gynecologic surgery, evidence is strongest to support use of LDUH. For patients with malignancy, a regimen of every 8 hour dosing should be maintained.

Additional patient related risk factors may place younger patients and/or those with more minor procedures into the high-risk category. (See "Guide to Risk Stratification" section in Annotation #5 in the original guideline document for more information.)

Evidence supporting this recommendation is of classes: A, C, D, M, R

Mechanical methods include elastic stockings (ES) and intermittent pneumatic compression (IPC), and more recently, foot pumps (FP). Both appear to augment venous return and induce the fibrinolytic system. Less often commented upon is that different devices vary in their augmentation of venous blood flow.

In moderate-risk patients, elastic stockings and IPC may be considered an alternative to LDUH bearing in mind that there is less data to support this strategy, that hemorrhagic complications are low with both strategies, and that compliance may be a significant problem when relying on IPC for VTE prophylaxis.

Refer to the original guideline for more information.

Evidence supporting this recommendation is of classes: A, B, C, D, M, R

Neuraxial Blockade

General Guidelines:

1. Neuraxial blockade should generally be avoided in patients with a clinical bleeding disorder.
2. For patients on other medicines that affect bleeding (aspirin, other platelet inhibitors or anticoagulants): insertion of the spinal needle should be delayed until the anticoagulant effect is minimal (i.e., at least 8 to 12 hours after a prophylactic dose of LMWH or LDUH).
3. Anticoagulant prophylaxis should be avoided or delayed if there was a hemorrhagic aspirate at the time of needle insertion.

4. All patients who receive neuraxial blockade should be monitored closely for developing back pain or signs and symptoms of spinal cord compression.
5. Anticoagulant prophylaxis should be delayed at least two hours following spinal or epidural catheter insertion.
6. For patients at moderate, high, or very high risk for VTE, a different form of analgesia should be used.
7. Removal of the epidural catheter should occur when the anticoagulant effect is at its minimum (approximately 2 hours before the next scheduled injection).
8. Consider obtaining a platelet count, international normalized ratio (INR), activated partial thromboplastin time (aPTT), or other appropriate test to assess coagulation status on the day the epidural catheter is removed.

Neuraxial blockade (spinal or epidural anesthesia) is a valuable tool for both anesthesiologists and surgeons alike. The Cochrane Reviews and other sources have listed the usefulness of neuraxial blockade for both intraoperative anesthesia as well as postoperative analgesia. There are groups of patients that demonstrate improved morbidity and mortality with the use of regional rather than general anesthesia. Similarly the usefulness of VTE prophylaxis in preventing morbidity and mortality in surgical patients has been well established. However, there is concern about an increased risk of perispinal hematoma in patients receiving antithrombotic medications for VTE prophylaxis in the setting of neuraxial blockade.

Perispinal hematoma is a rare but serious complication of neuraxial blockade. Thus, it is important to consider both the use and the timing of antithrombotic medications in these patients.

### Antiplatelet agents with neuraxial blockade

There is sufficient data to support that non-steroidal anti-inflammatory drug (NSAID) and aspirin used both preoperatively and perioperatively do not influence the risk of perispinal hematoma.

The actual risk of perispinal hematoma in patients receiving GP IIb/IIIa inhibitors is unknown, but reviews indicate GP IIb/IIIa should not be used within 3 to 4 weeks of neuraxial blockade. Labeling suggests discontinuation of ticlopidine 14 days and clopidogrel 7 days prior to any neuraxial blockade.

### Warfarin with neuraxial blockade

There is no increased risk of perispinal hematoma in patients receiving warfarin postoperatively. However, the mean time to catheter removal was approximately 36 hours and the majority of patients did not have an INR above 1.5 at the time of removal in the study by Horlocker detailed in the original guideline document.

The ASRA (American Society of Regional Anesthesia) guideline indicates removal of catheter when INR is less than 1.5 with INR checks perioperatively

and daily if the first dose of coumadin was given greater than 24 hours preoperatively.

Heparin with neuraxial blockade

In general, the most critical time for risk of perispinal hematoma is with indwelling catheter insertion and removal.

Low-dose unfractionated heparin (LDUH) for VTE prophylaxis in patients receiving neuraxial blockade does not appear to have significant risk. The ASRA guideline indicates no change in approach to patients receiving LDUH. If the patient has received four or more days of LDUH preoperatively, they should be assessed for heparin-induced thrombocytopenia (HIT). The work group recommends the insertion or removal of an indwelling catheter be 8 to 12 hours after the last dose of LMWH or LDUH.

Low molecular weight heparin (LMWH) for VTE prophylaxis in patients receiving neuraxial blockade has some potential issues. In 1997, the US Food and Drug Administration (FDA) issued a physician advisory for LMWH and risk of spinal hematoma. They described 43 U.S. patients who developed perispinal hematoma after receiving the LMWH enoxaparin for VTE prophylaxis. Many of these patients developed permanent neurologic sequelae despite 65% receiving aggressive therapy and laminectomy. The median age of the patients was 78 years, and 78% of the patients were women. The potential risk factors were many, including presence of underlying hemostatic disorder, traumatic needle or catheter insertion, repeated needle insertion attempts or a bloody return in the catheter, catheter insertion or removal in the setting of significant anticoagulation, concurrent use of other antithrombotic agents, use of continuous epidural catheters, anticoagulant dosages and vertebral column abnormalities. There were not large enough patient numbers to develop prevalence data nor establish relative risk for any of the individual risk factors. Therefore, no specific conclusions could be made.

10. Very High VTE Risk

Very high-risk patients include:

- Major surgery in patients over 40 years of age with a history of prior VTE or cancer
- All hip and knee arthroplasty patients
- All hip fracture patients
- All major trauma patients
- All spinal cord injury patients

Without prophylaxis, very high-risk VTE patients have a 10 to 20% proximal DVT risk, a 4 to 10% clinical PE risk, and a 0.2 to 0.5% risk of fatal PE.

See Annotation #5 for more information.

Evidence supporting this information is of class: R

11. Prophylaxis Plan for Very High VTE Risk

All high VTE risk patients should receive patient education, early ambulation, elastic support stockings, intermittent pneumatic compression if immobilized, and anticoagulation prophylaxis unless contraindicated. For short-term prophylactic anticoagulation, there are relatively few conditions with excessive bleeding risk or other considerations that would contraindicate anticoagulation. Acceptable anticoagulation regimens include LMWH, fondaparinux, and adjusted dose warfarin to keep the international normalized ratio (INR) between 2.0 and 3.0. Aspirin and LDUH are not recommended. Consideration should be given to extending the period of anticoagulation prophylaxis beyond hospitalization, depending on the length of hospital stay. If anticoagulation is contraindicated, placement of an inferior vena cava filter should be considered in this patient group. Refer to the table in Annotation #11 of the original guideline document for details on pharmacotherapy for patients stratified to very high-risk of VTE.

Supportive Comments for Pharmacotherapy of Patients at Very High VTE Risk:

1. Warfarin is contraindicated in the first trimester of pregnancy. Refer to the Institute for Clinical systems Improvement (ICSI) Anticoagulation Therapy Supplement for further dosing information.
2. Warfarin alone without concomitant heparin has been shown effective in prevention of venous thromboembolism for patients requiring hip replacement surgery.
3. Warfarin may be used when the patient has a history of heparin-induced thrombocytopenia (HIT)
4. LMWHs cause less HIT than LDUH. There is early evidence to support the use of fondaparinux in HIT although further confirmatory studies are needed.
5. LMWH should be adjusted to prophylactic doses for patients with a creatinine clearance less than 30 mL/min. The manufacturer recommended dose of enoxaparin is 30 mg daily in this population; the manufacturer of dalteparin does not list a similar dose recommendation.
6. In patients who have undergone total knee replacement, total hip replacement, and hip fracture repair, a minimum of 10 days of anticoagulation prophylaxis is recommended. For patients undergoing total hip replacement or hip fracture repair a recommendation of extended prophylaxis of 28 to 35 days of postoperative anticoagulation should be given.
7. Dalteparin and enoxaparin are started 12 to 24 hours post-op depending on physician determination of adequate hemostasis.
8. Fondaparinux is the only anticoagulant with a Federal Drug and Food Administration (FDA)-approved indication for hip fracture.
9. Aspirin and LDUH are not recommended for very high-risk patients.
10. For trauma patients, contraindications to early pharmacotherapy include intracranial bleeding, incomplete spinal cord injury, ongoing, uncontrolled bleeding, and uncorrected coagulopathy.

See "Other VTE risk factors that play an additive role" and "Guide to Risk Stratification" sections in Annotation #5 of the original guideline for more information.

Evidence supporting this recommendation is of classes: A, B, C, D, R

## Hospitalized Medical Patient Algorithm Annotations

12. Adult Admitted to an Acute Care Hospital for a Medical Condition

All patients admitted for medical reasons should be evaluated for risk of VTE development.

See the National Guideline Clearinghouse (NGC) summary of Institute for Clinical Systems Improvement (ICSI) guideline Diagnosis and Treatment of Chest Pain and Acute Coronary Syndrome (ACS) guideline for recommendations on prophylaxis for patients suspected of MI.

See the NGC summary of ICSI guideline Diagnosis and Initial Treatment of Ischemic Stroke for recommendations on prophylaxis for patients suspected of cerebrovascular accident (CVA).

Appropriate prophylaxis should be initiated for patients deemed to be at risk.

14. High Risk of VTE?

Refer to the original guideline document for information on patients considered at high risk for VTE for whom pharmacologic prophylaxis should be considered.

See also Appendix A in the original guideline, "Heart Failure Classification" for information on the classifications of heart failure and comparison to American College of Cardiology/American heart Association (ACC/AHA) 2001 staging.

15. Prophylaxis Plan for Low VTE Risk

All patients should receive patient education and early ambulation. Education should include signs and symptoms of VTE. Encourage early and frequent ambulation with flexion/extension exercises for the ankles.

Early mobilization is a therapy to enhance a patient's well being. This therapy may result in shorter hospitalization due to a specific mobilization program utilized to help patients start regaining their strength. This practice may start mobilization earlier than normally practiced.

Physical therapy may need to be involved as soon as possible and mobilization will start by sitting and progress to walking if applicable. This should be done every shift or more based on how the patient tolerates mobilization.

Evidence supporting this recommendation is of class: R

16. Contraindications to Antithrombotic Prophylaxis?

Pharmacologic prophylaxis is not without risk. Patients should be evaluated for an increase risk of bleeding.

The following are contraindications for pharmacologic prophylaxis:

a. Extreme thrombocytopenia
b. History of heparin-induced thrombocytopenia (HIT) is contraindicated for use of heparins.
c. Uncontrolled hypertension (systolic >200, diastolic >120)
d. Bacterial endocarditis
e. Active hepatitis or hepatic insufficiency
f. Other conditions that could increase the risk of bleeding

See the ICSI Anticoagulation Therapy Supplement for more information.

17. Prophylaxis Plan

Patients with a high risk for developing VTE who have contraindications for pharmacologic prophylaxis should receive patient education and early ambulation.

Though the work group is not aware of any trials of mechanical prophylaxis, it is the recommendation of this group that all patients admitted to the hospital for medical reasons ambulate as early and as often as possible. Elastic stockings may also be considered. Intermittent pneumatic compression is often annoying to the patient and should be reserved for medical patients who are confined to bed and unable to ambulate.

18. Prophylaxis Plan for High VTE Risk

Key Points:

- Patients at high risk for VTE and without contraindication to antithrombotic should receive anticoagulation prophylaxis beginning at admission and continuing while risk continues.
- Patients with renal insufficiency (creatinine clearance [CCL] <30 mL/min) should receive unfractionated heparin or LMWH adjusted for renal insufficiency.
- Patients at high-risk for VTE who have a previous history of heparin-induced thrombocytopenia (HIT) should be managed by an anticoagulation specialist.

See Appendix B, "Summary of VTE Prophylaxis Trials" in the original guideline.

Refer to the Table in Annotation #18 of the original guideline that summarizes pharmacotherapy for medically-ill patients at high risk for VTE.

Evidence supporting this recommendation is of classes: A, R

Definitions:

Conclusion Grades:

Grade I: The evidence consists of results from studies of strong design for answering the question addressed. The results are both clinically important and consistent with minor exceptions at most. The results are free of any significant doubts about generalizability, bias, and flaws in research design. Studies with negative results have sufficiently large samples to have adequate statistical power.

Grade II: The evidence consists of results from studies of strong design for answering the question addressed, but there is some uncertainty attached to the conclusion because of inconsistencies among the results from the studies or because of minor doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from weaker designs for the question addressed, but the results have been confirmed in separate studies and are consistent with minor exceptions at most.

Grade III: The evidence consists of results from studies of strong design for answering the question addressed, but there is substantial uncertainty attached to the conclusion because of inconsistencies among the results of different studies or because of serious doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from a limited number of studies of weak design for answering the question addressed.

Grade Not Assignable: There is no evidence available that directly supports or refutes the conclusion.

Classes of Research Reports:

A. Primary Reports of New Data Collection:

Class A:

- Randomized, controlled trial

Class B:

- Cohort study

Class C:

- Non-randomized trial with concurrent or historical controls
- Case-control study
- Study of sensitivity and specificity of a diagnostic test
- Population-based descriptive study

Class D:

- Cross-sectional study
- Case series
- Case report

B. Reports that Synthesize or Reflect upon Collections of Primary Reports:

Class M:

- Meta-analysis
- Systematic review
- Decision analysis
- Cost-effectiveness analysis

Class R:

- Consensus statement
- Consensus report
- Narrative review

Class X:

- Medical opinion

### CLINICAL ALGORITHM(S)

Detailed and annotated clinical algorithms are provided for

- Venous Thromboembolism Prophylaxis for Hospitalized Surgical/Trauma Patients
- Venous Thromboembolism Prophylaxis for Hospitalized Medical Patients

## EVIDENCE SUPPORTING THE RECOMMENDATIONS

### TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The guideline contains an annotated bibliography and discussion of the evidence supporting each recommendation. The type of supporting evidence is classified for selected recommendations (see "Major Recommendations").

In addition, key conclusions contained in the Work Group's algorithm are supported by a grading worksheet that summarizes the important studies pertaining to the conclusion. The type and quality of the evidence supporting these key recommendations (i.e., choice among alternative therapeutic approaches) is graded for each study.

## BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

### POTENTIAL BENEFITS

- Appropriate assessment for venous thromboembolism (VTE) risk

- Increased rate of adult hospitalized patients receiving appropriate pharmacological and/or mechanical prophylaxis
- Increased rate of adult hospitalized patients receiving education for VTE
- Increased rate of adult hospitalized patients who begin early and frequent ambulation to reduce VTE risk

### POTENTIAL HARMS

#### Side Effects of Anticoagulant Medications (Low Dose Unfractionated Heparin [LDUH] and Low Molecular Weight Heparin [LMWH])

- Bleeding (major and minor)
- Heparin-induced thrombocytopenia (LMWH causes less heparin-induced thrombocytopenia than LDUH)

#### Side Effects of Mechanical Methods of Venous Thromboembolic Prophylaxis

- Side effects of elastic stockings are rare, although a proper fit, particularly in the obese, may be difficult in 10 to 15% of patients.
- Complications with intermittent pneumatic compression devices include perineal neuropathy and compartment syndrome with lithotomy position and weight loss as risk factors. Compliance may also be significantly more difficult than with heparin regimens.

#### Subgroups Most Likely to be Harmed

There is some evidence that LMWH may need to be adjusted at prophylactic doses in severe renal impairment (Creatinine clearance <30 mL/minute).

Refer to "Neuraxial Blockade" section in Annotation #9 for more information.

## CONTRAINDICATIONS

### CONTRAINDICATIONS

- For trauma patients, contraindications to early pharmacotherapy include intracranial bleeding; incomplete spinal cord injury; ongoing, uncontrolled bleeding; and uncorrected coagulopathy
- Contraindications to warfarin include the first trimester of pregnancy.
- Contraindications to antithrombotic prophylaxis:
    - Extreme thrombocytopenia
    - History of heparin-induced thrombocytopenia
    - Uncontrolled hypertension (systolic >200, diastolic >120)
    - Bacterial endocarditis
    - Active hepatitis or hepatic insufficiency
    - Other conditions that could increase the risk of bleeding

## QUALIFYING STATEMENTS

### QUALIFYING STATEMENTS

- These clinical guidelines are designed to assist clinicians by providing an analytical framework for the evaluation and treatment of patients and are not intended either to replace a clinician's judgment or to establish a protocol for all patients with a particular condition. A guideline will rarely establish the only approach to a problem.
- This clinical guideline should not be construed as medical advice or medical opinion related to any specific facts or circumstances. Patients are urged to consult a health care professional regarding their own situation and any specific medical questions they may have.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

Once a guideline is approved for release, a member group can choose to concentrate on the implementation of that guideline. When four or more groups choose the same guideline to implement and they wish to collaborate with others, they may form an action group.

In the action group, each medical group sets specific goals they plan to achieve in improving patient care based on the particular guideline(s). Each medical group shares its experiences and supporting measurement results within the action group. This sharing facilitates a collaborative learning environment. Action group learnings are also documented and shared with interested medical groups within the collaborative.

Currently, action groups may focus on one guideline or a set of guidelines such as hypertension, lipid treatment, and tobacco cessation.

The following detailed measurement strategies are presented to help close the gap between clinical practice and the guideline recommendations. Refer to the "Major Recommendations" field for information regarding the annotations listed below.

Priority Aims and Suggested Measures

1. Increase the percentage of hospitalized adult patients (18 years and older) who are assessed for venous thromboembolism (VTE) risk. (Annotation #5)

   Possible measure for accomplishing this aim:

   a. Percentage of adult hospitalized patients (18 years and older) who have a VTE assessment documented in their chart
2. Increase the percentage of hospitalized adult patients (18 years and older) who are at risk of VTE who have received education for VTE that includes:

VTE risk signs and symptoms and treatment/prophylaxis methods available (Annotations #7, 9, 11, 14, 18, 19)

Possible measure for accomplishing this aim:

a. Percentage of hospitalized patients who are at risk for VTE, who have documented education for VTE in their chart

3. Increase the percentage of hospitalized adult patients who begin early and frequent ambulation to reduce VTE risk (Annotation #7)

Possible measure for accomplishing this aim:

a. Percentage of hospitalized patients who have documentation of early and frequent ambulation recorded in the medical record (Annotations #7, 9, 11, 14, 18)

4. Increase the percentage of hospitalized adult patients (18 years and older) receiving appropriate pharmacological and/or mechanical prophylaxis treatment or a combination of both (Annotations #7, 9, 11)

Possible measure for accomplishing this aim:

a. Percentage of surgical/trauma hospitalized adult patients with low, moderate/high, or very high-risk for VTE who have received appropriate prophylaxis as defined by the guideline (Annotations #7, 9, 11)
b. Percentage of medical hospitalized adult patients with low or very high risk for VTE who have received appropriate prophylaxis as defined by the guideline (Annotations #14, 19)

At this point in development for this guideline, there are no specifications written for possible measures listed above. The Institute for Clinical Systems Improvement (ICSI) will seek input from the medical groups on what measures are of most use as they implement the guideline. In a future revision of the guideline, measurement specifications may be included.

## Key Implementation Recommendations

The following system changes were identified by the guideline work group as key strategies for health care systems to incorporate in support of the implementation of this guideline.

1. Medical groups and hospitals are encouraged to develop a formal strategy that addresses the prevention of thromboembolic complications.
2. Medical groups and hospitals are encouraged to develop systems that support:
    - Early identification of patients at risk for VTE development (possibly through use of order sets or similar tools)
    - Appropriate prophylaxis initiation (possibly through order sets and/or anticoagulation protocols)
    - Patient education to include documentation of the patient's own awareness of their risk for VTE, signs and symptoms of VTE and

when/how to seek treatment, and demonstrated understanding of the prescribed anticoagulation regimen

### IMPLEMENTATION TOOLS

Clinical Algorithm
Pocket Guide/Reference Cards

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Staying Healthy

### IOM DOMAIN

Effectiveness
Patient-centeredness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

Institute for Clinical Systems Improvement (ICSI). Venous thromboembolism prophylaxis. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2005 Jun. 45 p. [80 references]

### ADAPTATION

Not applicable: The guideline was not adapted from another source.

### DATE RELEASED

2003 Oct (revised 2005 Jun)

### GUIDELINE DEVELOPER(S)

Institute for Clinical Systems Improvement - Private Nonprofit Organization

### GUIDELINE DEVELOPER COMMENT

Organizations participating in the Institute for Clinical Systems Improvement (ICSI): Affiliated Organizations participating in the Institute for Clinical Systems Improvement (ICSI): Affiliated Community Medical Centers, Allina Medical Clinic, Altru Health System, Aspen Medical Group, Avera Health, CentraCare, Columbia

Park Medical Group, Community-University Health Care Center, Dakota Clinic, ENT Specialty Care, Fairview Health Services, Family HealthServices Minnesota, Family Practice Medical Center, Gateway Family Health Clinic, Gillette Children's Specialty Healthcare, Grand Itasca Clinic and Hospital, HealthEast Care System, HealthPartners Central Minnesota Clinics, HealthPartners Medical Group and Clinics, Hutchinson Area Health Care, Hutchinson Medical Center, Lakeview Clinic, Mayo Clinic, Mercy Hospital and Health Care Center, MeritCare, Mille Lacs Health System, Minnesota Gastroenterology, Montevideo Clinic, North Clinic, North Memorial Care System, North Suburban Family Physicians, Northwest Family Physicians, Olmsted Medical Center, Park Nicollet Health Services, Pilot City Health Center, Quello Clinic, Ridgeview Medical Center, River Falls Medical Clinic, Saint Mary's/Duluth Clinic Health System, St. Paul Heart Clinic, Sioux Valley Hospitals and Health System, Southside Community Health Services, Stillwater Medical Group, SuperiorHealth Medical Group, University of Minnesota Physicians, Winona Clinic, Ltd., Winona Health

ICSI, 8009 34th Avenue South, Suite 1200, Bloomington, MN 55425; telephone, (952) 814-7060; fax, (952) 858-9675; e-mail: icsi.info@icsi.org; Web site: www.icsi.org.

## SOURCE(S) OF FUNDING

The following Minnesota health plans provide direct financial support: Blue Cross and Blue Shield of Minnesota, HealthPartners, Medica, Metropolitan Health Plan, PreferredOne and UCare Minnesota. In-kind support is provided by the Institute for Clinical Systems Improvement's (ICSI) members.

## GUIDELINE COMMITTEE

Cardiovascular Steering Committee

## COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Work Group Members: Mark Morrow, MD (Work Group Leader) (Aspen Medical Group) (Internal Medicine); Rick Wehseler, MD (Affiliated Community Medical Centers) (Family Medicine); John Heit, MD (Mayo Clinic) (Hematology); Bruce Burnett, MD (Park Nicollet Health Services) (Internal Medicine); Peter Friedlieb, MD (Grand Itasca Clinic and Hospital) (Internal Medicine); Karyl Tammel, RN (May Clinic) (Nursing); Paul Johnson, MD (Park Nicollet Health Services) (Orthopedic Surgery); Kim Cartie, PharmD (HealthPartners Medical Group) (Pharmacy); Sherri Jobin, PharmD (HealthEast Care System) (Pharmacy); Jill Strykowski, RPh, MS (Park Nicollet Health Services) (Pharmacy); Beth Green, MBA, RRT (Institute for Clinical Systems Improvement) (Implementation/Measurement Advisor); Brent Metfessel, MD, MPH (Institute for Clinical Systems Improvement) (Evidence Analyst); Sherri Huber, MT (ASCP) (Institute for Clinical Systems Improvement) (Facilitator)

## FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

In the interest of full disclosure, Institute for Clinical Systems Improvement (ICSI) has adopted the policy of revealing relationships work group members have with

companies that sell products or services that are relevant to this guideline topic. The reader should not assume that these financial interests will have an adverse impact on the content of the guideline, but they are noted here to fully inform users. Readers of the guideline may assume that only work group members listed below have potential conflicts of interest to disclose.

Bruce Burnett, MD is a member of the speakers bureau for Astra Zeneca, Aventis, Bristol Myers Squibb; a consultant for Aventis, Astra Zeneca, and Glaxo SmithKline; receives research support from Astra-Zeneca.

John Heit, MD receives honoraria from Sandofi-Aventis, a consultant for Sandofi-Aventis.

No other work group members have potential conflicts of interest to disclose.

ICSI's conflict of interest policy and procedures are available for review on ICSI's website at www.icsi.org.

## GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Venous thromboembolism prophylaxis for surgical/trauma patients. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2003 Oct. 39 p.

## GUIDELINE AVAILABILITY

Electronic copies: Available from the Institute for Clinical Systems Improvement (ICSI) Web site.

Print copies: Available from ICSI, 8009 34th Avenue South, Suite 1200, Bloomington, MN 55425; telephone, (952) 814-7060; fax, (952) 858-9675; Web site: www.icsi.org; e-mail: icsi.info@icsi.org.

## AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- ICSI pocket guidelines. April 2004 edition. Bloomington (MN): Institute for Clinical Systems Improvement, 2004. 404 p.

Print copies: Available from ICSI, 8009 34th Avenue South, Suite 1200, Bloomington, MN 55425; telephone, (952) 814-7060; fax, (952) 858-9675; Web site: www.icsi.org; e-mail: icsi.info@icsi.org.

Additionally, a measurement tool, "Optional Medical Record Review Format for ACE Inhibitor Use" is available in the "Support for Implementation" section of the original guideline document.

## PATIENT RESOURCES

None available

## NGC STATUS

This NGC summary was completed by ECRI on April 29, 2004. It was updated by ECRI on September 16, 2005.

## COPYRIGHT STATEMENT



# DISCLAIMER

## NGC DISCLAIMER

The National Guideline Clearinghouse™ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at http://www.guideline.gov/about/inclusion.aspx.

NGC, AHRQ, and its contractor ECRI make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect

those of NGC, AHRQ, or its contractor ECRI, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.



Date Modified: 12/19/2005